PulmCrit- APRV: Resurrection of the open-lung strategy?

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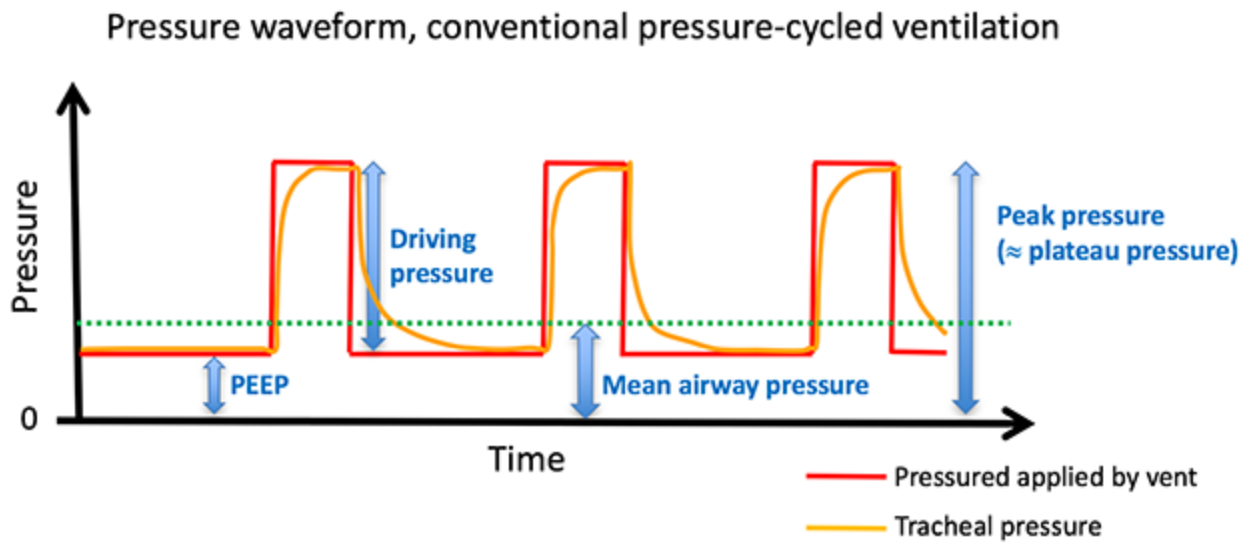
You are here: Home / PULMCrit / PulmCrit- APRV: Resurrection of the open-lung strategy?

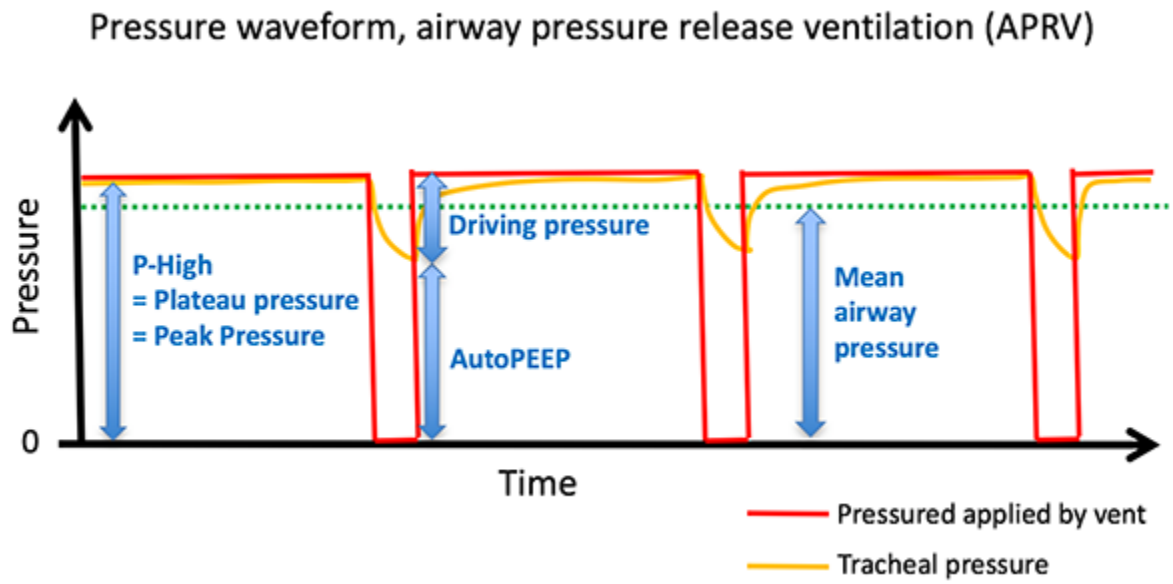
Airway Pressure Release Ventilation (APRV): Solution to the open-lung challenge?

Open-lung ventilation refers to the concept of recruiting the lung and then ventilating gently with small tidal volumes, to avoid either over-distension or atelectotrauma (lung damage from cyclical opening/closing of alveoli). ARDSnet low tidal-volume ventilation was a success for the open lung concept. However, subsequent efforts to advance this concept further have floundered, with several failed attempts to manipulate PEEP. A recent editorial in JAMA speculated about whether the open-lung strategy is dead (Sahetya 2017).

The obstacle to opening the lung using conventional ventilation is basic arithmetic. Opening the lung requires more PEEP. Driving pressure can be reduced a bit, but it can't be reduced too much without causing severe hypoventilation. Therefore, increasing the PEEP forces the plateau pressure to rise (figure below). You can't have your cake and eat it too (high PEEP and low plateau).



APRV solves this problem by flipping the pressure curve upside-down. A *single* pressure (P-High) is used both to recruit the lungs and also as the driving pressure for exhalation. This allows achieving a high mean airway pressure with a relatively low plateau pressure:



Great idea, little hard evidence.

APRV is conceptually very appealing, for example:

- APRV is better tolerated than conventional low tidal-volume ventilation, obviating the need for paralytics and deep sedation. This may avoid complications such as myopathy and delirium. APRV is compatible with early-mobility initiatives (some videos from Maryland Shock Trauma feature patients walking on APRV).
- Diaphragmatic activity promotes recruitment and ventilation of the lung bases.
- Rapid release breaths may facilitate secretion clearance, reducing the risk of ventilator-associated pneumonia.
- Active breathing may improve venous return and cardiac output.
- Ventilator-induced lung injury might be a product of the tidal volume multiplied by the frequency of ventilation (which determines the total *energy* absorbed by the lung; figure below). Since APRV involves relatively infrequent release breaths and a lower minute

ventilation than conventional ventilation, this should make APRV more lung-protective (1).

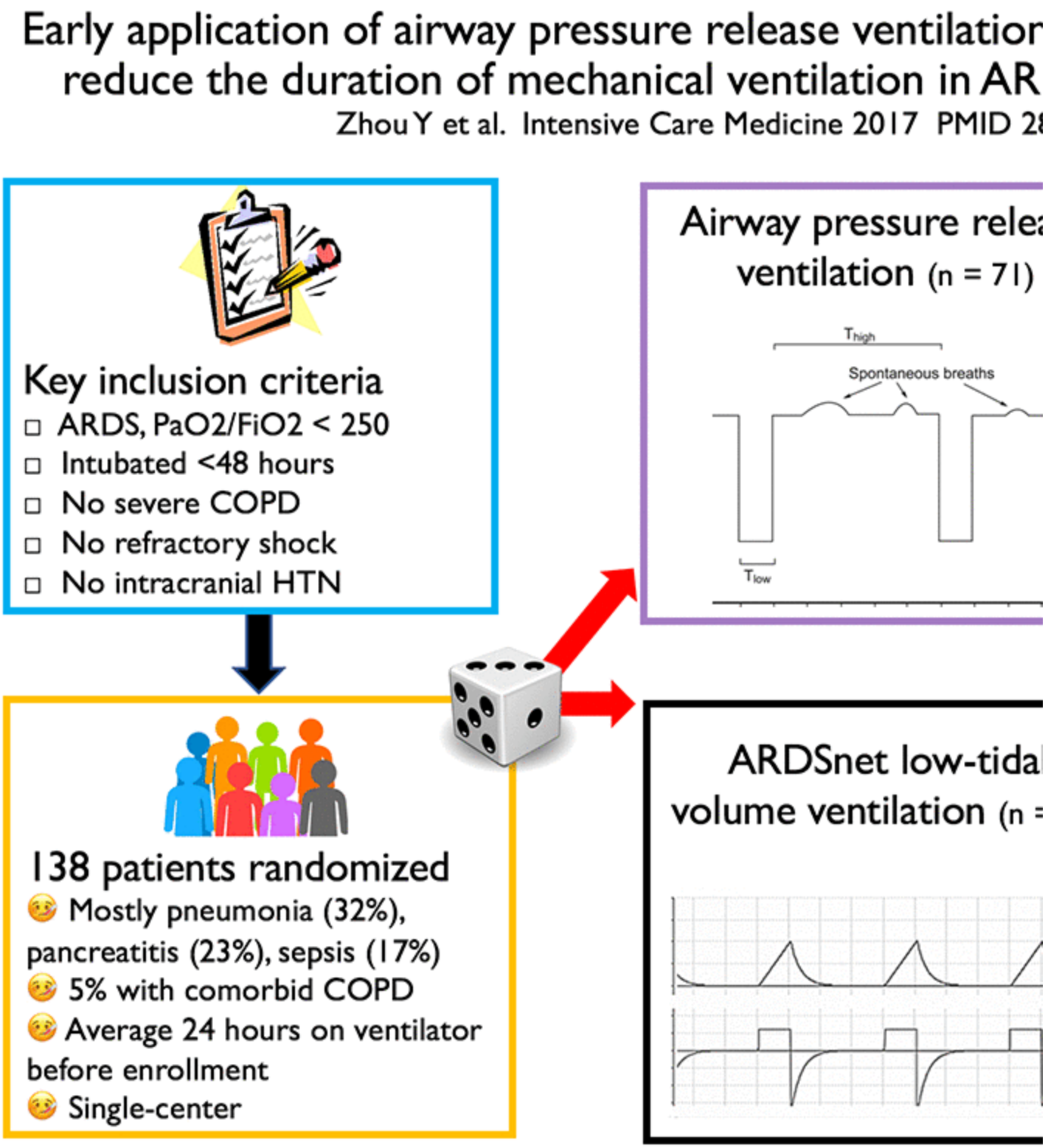
Vent-induced lung injury might depend on *both* how lung-protective each breath is (power in each punch) multiplied by the frequency of breaths (total number of punches). NB: Don't beat up the lung.

However, until recently there were several drawbacks to APRV:

- Lack of prospective RCT evidence showing a benefit of APRV versus conventional low tidal-volume ventilation.
- Lack of evidence in the medical ICU (most experience originates from the surgical ICU).
- Use of large tidal volumes in the release breaths (>8-10 cc/kg) seems to violate the principles of lung-protective ventilation.
- Weaning APRV can be a tedious process of gradually reducing the pressure.

This has led to a paradoxical situation, where APRV is often used in *surgical* ICUs but not *medical* ICUs. APRV may be viewed as a "new" technique by medical intensivists, whereas it's been used for decades in surgical ICUs with great results (Andrews 2013). A fresh RCT may help resolve this...

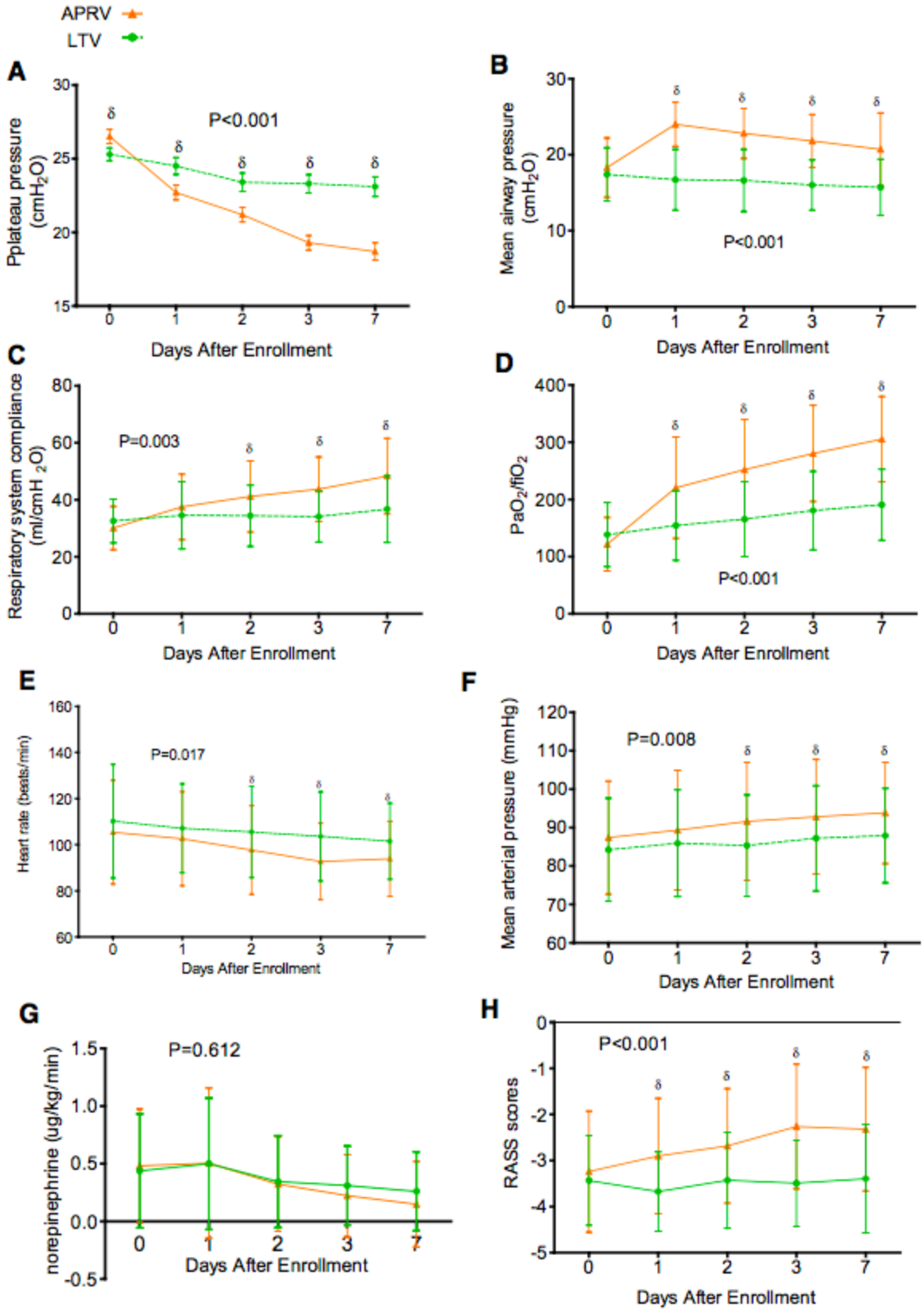
Zhou et al 2017



This is by far the largest RCT of APRV to date. Patients with ARDS were randomized to receive APRV versus low tidal-volume ventilation. The primary endpoint was the number of ventilator-free days, which was dramatically greater in the APRV group. Patients treated with APRV required fewer additional therapies (proning, paralysis, and recruitment).

Main outcome variables	APRV ($n = 71$) [b]	LTV ($n = 67$) [b]	*P* value
No. of days of ventilation	8 [5–14]	15 [7–22]	0.001
No. of ventilator-free days at 28 days	19 [8–22]	2 [0–15]	<0.001
Successful extubation	47 (66.2%)	26 (38.8%)	0.001
Tracheostomy	9 (12.7%)	20 (29.9%)	0.013
Length of ICU stay (days)	15 [8–21]	20 [10–32]	0.015
Pneumothorax between day 1 and day 28[a]	3 (4.2%)	7 (10.4%)	0.199
Death during the ICU stay	14 (19.7%)	23 (34.3%)	0.053
Length of hospital stay (days)	21 [14–30]	27 [18–41]	0.055
Death during the hospital stay	17 (23.9%)	25 (37.3%)	0.088
Other supportive therapies			
Neuromuscular blocker	2 (2.8%)	9 (13.4%)	0.021
Recruitment maneuvers	4 (5.6%)	11 (16.4%)	0.042
Prone position	2 (2.8%)	10 (14.9%)	0.012
Inhaled nitric oxide	1 (1.4%)	1 (1.5%)	1.000
High-frequency oscillatory ventilation	1 (1.4%)	3 (4.5%)	0.355

APRV was well tolerated hemodynamically, with higher blood pressure and lower heart rates. Patients with APRV were more awake, receiving less sedative and pain medication:



This study does have limitations:

- Single-center design.
- Open-label (unavoidable, given differences between APRV and conventional ventilation).
- Within the APRV group, respiratory therapists were allowed to titrate analgesics and sedatives to promote spontaneous breathing. More intensive titration of sedating medications

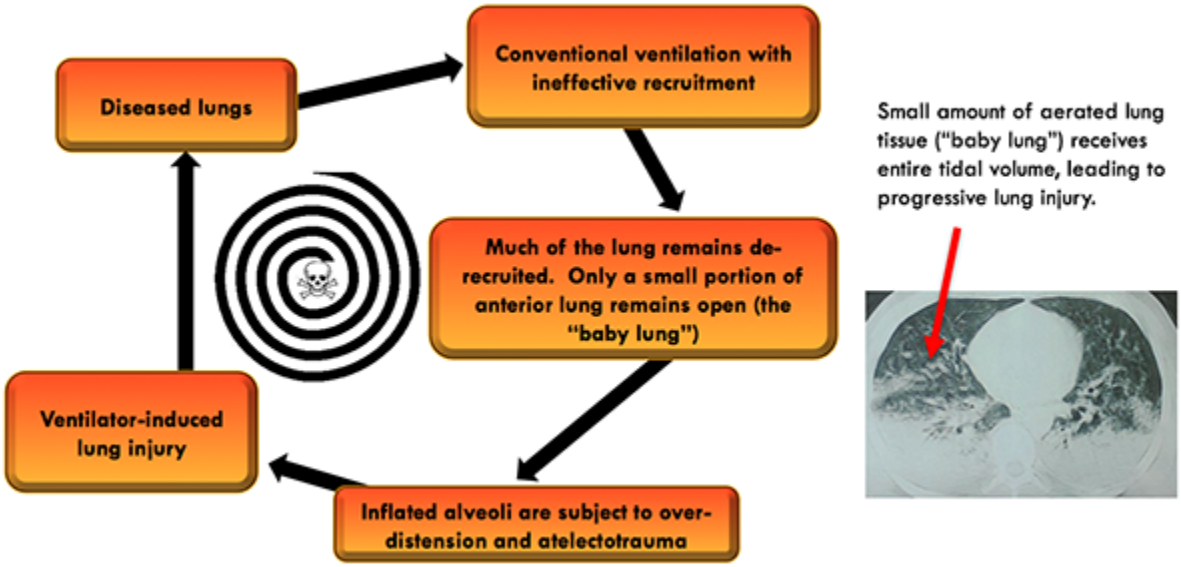
may have promoted lower levels of sedation and earlier extubation.
- The APRV protocol may require more effort, causing patients to receive more attention. However, this phenomenon might be generalizable to actual practice as well.

Devil in the details

Although APRV is often considered as a single "intervention," there are innumerable ways to perform APRV. Several components of the APRV protocol used by these authors deserve attention:

#1: Limiting P-High

When patients are placed on conventional ventilation, they often wind up in the vicious cycle shown below. The sicker they are, the higher the pressures they require. Higher pressures lead to worsening lung injury, and so on as the ventilator beats up the lung:



The protocol these authors used did some clever things to avoid this:

- The P-High was capped at 30 cm. This prevents patients from ever being exposed to extremely high levels of pressure.
- Persistent hypoxemia was managed by increasing P-Low. Thus, the sickest patients would receive higher P-Low, which would *decrease* the driving pressure and *decrease* the tidal volume (maximizing lung protection).

Capping P-High at 30 cm is controversial. It is appealing, because it could avoid barotrauma and cor pulmonale. However, it is possible that a P-High above 30 cm might be required to manage patients with supermorbid obesity. A recent survey of respiratory therapists from various institutions showed that practice regarding P-High is enormously variable (below, Miller 2017). This survey does suggest that capping P-High at 30 cm is possible, because it was the practice at nine hospitals.

Table 2. Airway Pressure Release Ventilation Settings

Setting	*n* (%)	95% CI
What is the maximum allowed P high? (n = 47)		
35 cm H_2O	21 (45)	0.31–0.59
30 cm H_2O	9 (19)	0.11–0.33
40 cm H_2O	9 (19)	0.11–0.33
No limit	8 (17)	0.09–0.30

Miller AG et al. 2017 PMID 28588118

#2: Use of a positive P-low

Unlike many current APRV protocols, these authors used P-Low values above zero (starting at 5 cm, then titrated). Using a positive P-Low value may make this more lung-protective, because it could avoid de-recruitment and reduce the driving pressure. However, it is likely that using a P-low of zero with appropriately short T-low would achieve the same result.

#3: Achievement of low tidal volumes

One notable aspect of this protocol is that there were *no significant differences* in tidal volume comparing APRV versus conventional low tidal-volume ventilation (e.g. on the first day after randomization, both groups had an average tidal volume of 7 cc/kg). Their ability to achieve low tidal volumes using APRV likely reflects a combination of capping P-High, increasing P-Low, and meticulous titration of T-Low. Some APRV protocols generate large tidal volumes (>8-10 cc/kg), which has been an ongoing source of concern. The ability to achieve low tidal volume ventilation with APRV makes this protocol much more appealing because it adheres better to the principles of lung-protective ventilation (2).

#4: Weaning via transition from P-High 20cm to spontaneous breathing trial

In general, modern principles of ventilator liberation emphasize the use of a comfortable, *non-fatiguing* level of ventilator support punctuated by a daily spontaneous breathing trial. Patients who fail the spontaneous breathing trial are immediately returned to full ventilator support.

The authors point out that most APRV protocols currently violate this concept. Usually, APRV is gradually weaned with a slow reduction in the level of ventilator support. This is potentially suboptimal:

- For a patient who isn't ready to wean, gradually reducing the ventilator support risks leaving the patient for long periods of time at an inadequate level of support. This may cause insidious diaphragmatic fatigue, setting the patient back substantially (severe muscle fatigue often takes 1-2 days to recover).
- For a patient who is ready to wean, gradually reducing support at an arbitrary rate may delay extubation.

Therefore, the authors weaned patients by performing intermittent conventional spontaneous breathing trials (5-7 cm pressure support and 5 cm PEEP) after the patients were on a low level of APRV (20 cm P-Hi and 40% FiO2). This is a very aggressive approach, which would cause most providers to worry about de-recruitment. Nonetheless, in their hands it seemed to work.

The ideal way to wean APRV remains unclear, requiring further study. It's possible that a dichotomy exists regarding the ability to adjust P-High:

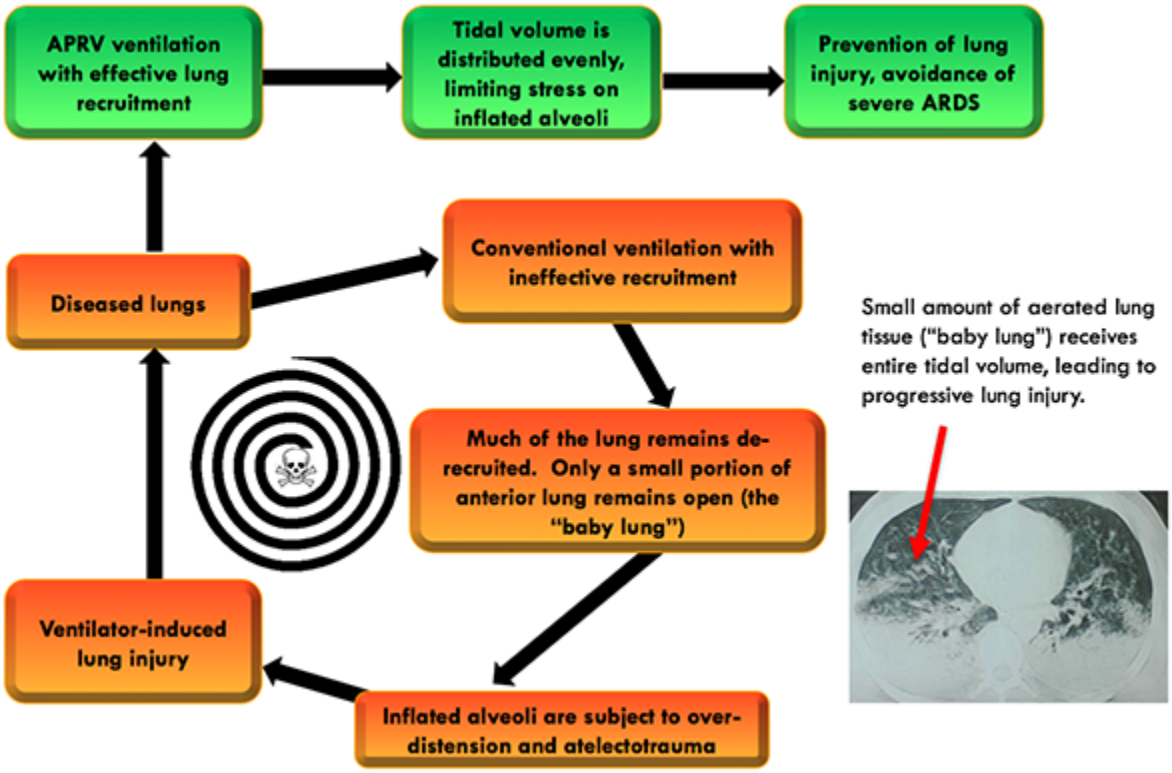
- While the patient is acutely ill, P-High must be adjusted very slowly to avoid de-recruitment.
- After the patient has stabilized for a few days and is recovering, APRV may be weaned off more rapidly.

#5. Early initiation of APRV

This study used APRV early in the patient's hospital course (within 48 hours of intubation). This may maximize the benefit of APRV for a few reasons:

- APRV works best when patients are relatively awake and not paralyzed. Alternatively, when APRV is used as a rescue mode, it is often applied to patients who are deeply sedated and paralyzed.
- The open-lung theory suggests that APRV may be more lung-protective than conventional ventilation. If so, it would make sense to initiate APRV early (rather than after the lungs have been injured by conventional mechanical ventilation).

This isn't a new concept: other authors have previously discussed that APRV ideally shouldn't be used as a salvage modality (Chatburn 2016). Indeed, emerging evidence supports the use of APRV up-front to stabilize the lung and *prevent* ARDS (Andrews 2013, Sadowitz 2016).

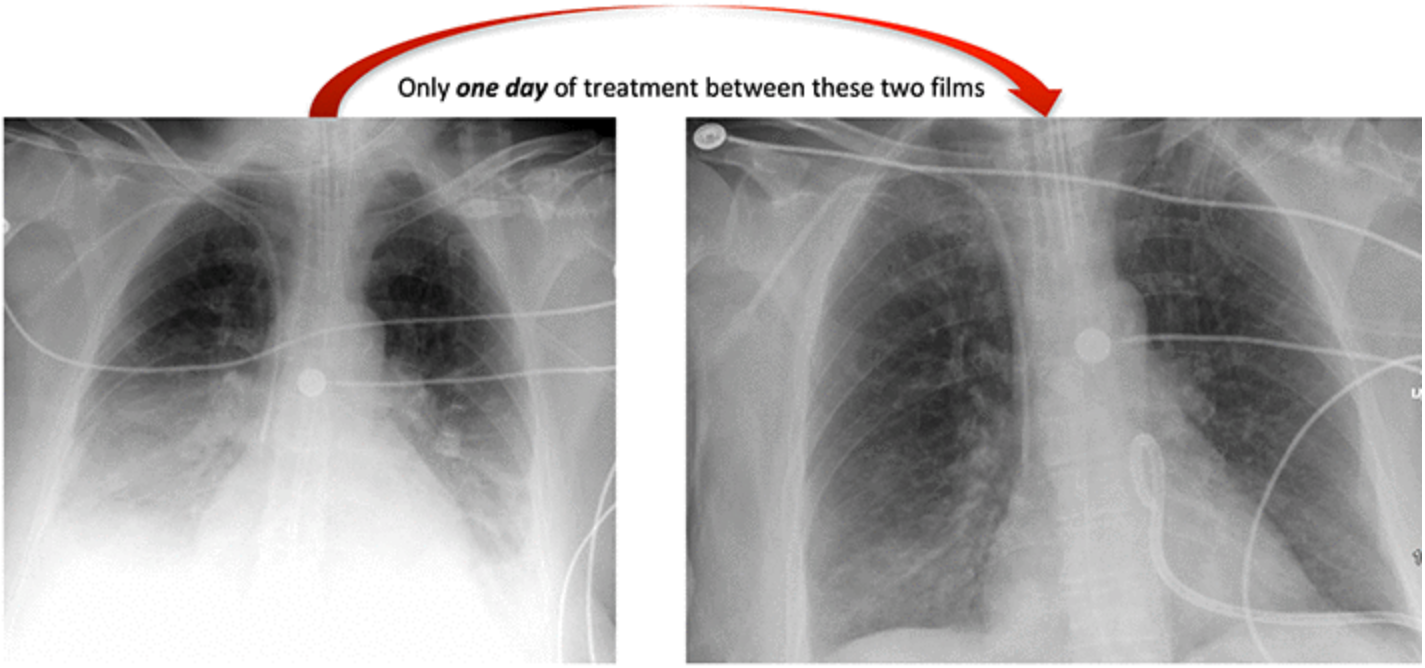


How should we set APRV?

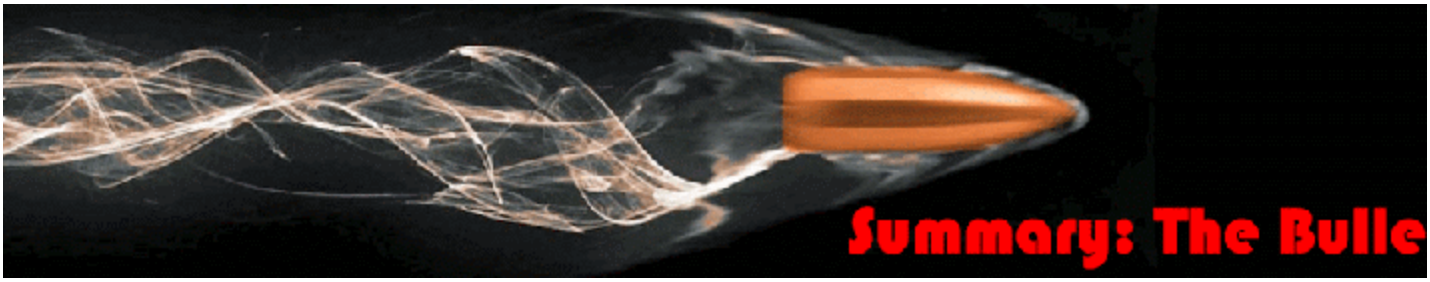
It remains unclear exactly how we should set APRV. One could argue that since Zhou has reported the best clinical outcomes in an RCT, we should replicate their protocol. However, some elements of their protocol may require further validation before widespread application (e.g. transitioning a patient directly from P-Hi of 20 cm to a conventional spontaneous breathing trial).

One attempt to create a guideline for APRV is shown here. This strives to combine some more traditional elements of APRV protocols with some of the more attractive features of Zhou's protocol

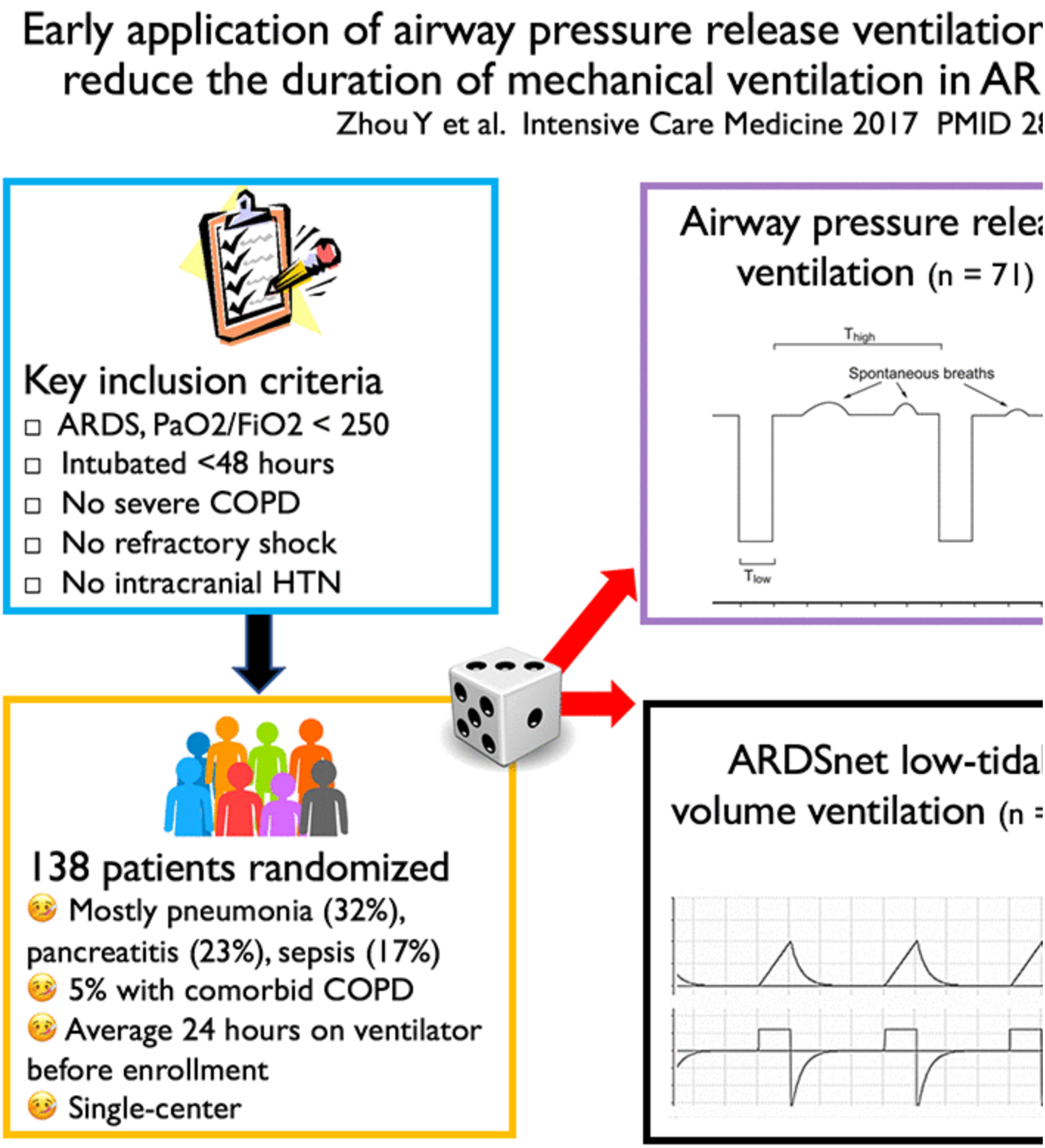
(e.g. limiting the P-High and achieving low tidal volumes). Based on positive outcomes from both Maryland Shock Trauma and Zhou et al. using different protocols, it's likely that a *variety* of different strategies would work fine.



De-resuscitative APRV: This man was transferred to Genius General Hospital after receiving 14 liters of crystalloid and becoming stuck on the ventilator at an outside hospital. He had anasarca, small-moderate effusions bilaterally and collapse of the bilateral lower lobes. Aggressive de-resuscitation was performed including simultaneous large-volume diuresis (~5 liters/day using indapamide plus furosemide), drainage of one effusion, and APRV to recruit the lung bases. While on APRV he was comfortable and awake, requiring no sedation and only a low-dose ketamine infusion for pain. He was successfully extubated and had an uneventful ICU course.



- Zhou et al. 2017 is the largest RCT to be performed on APRV. It shows benefit compared to conventional low tidal-volume ventilation in terms of liberation from the ventilator and fewer tracheostomies (figure below).
- This is a single-center study with significant limitations. It is premature to conclude that APRV is definitely superior to low tidal-volume ventilation. However, this study suggests that APRV is a legitimate front-line ventilator mode for patients with ARDS.
- *Early* use of APRV may allow avoidance of paralysis and deep sedation, facilitating more rapid weaning from ventilation. It's also possible that early application of APRV could avoid progressive ventilator-induced lung injury.
- The details of exactly how APRV is implemented are relevant. These authors avoided high peak pressure and high tidal volumes, which may have improved hemodynamic stability and lung protection.
- These authors weaned APRV very abruptly. Although this requires further study, it suggests that after the lung injury is improving and the patient has stabilized, APRV may be weaned relatively fast.



Related

- Zhou et al. Early application of airway pressure release ventilation may reduce the duration of mechanical ventilation in ARDS. Intensive Care Medicine 2017.
- APRV Guideline (PulmCrit)
- Commentary on Zhou study by Dr. Rhodri Handslip (ESICM blog)

- APRV Lecture by Nader Habashi (Maryland CCC project)
- APRV Ventilation Mode (Charles Bruen, Resus Review)
- APRV (LITFL blog)
- The Case of an Ugly Truth (EMNerd) Contains important discussion of 6 cc/kg vs 10 cc/kg tidal volumes.

Notes

1. APRV ventilation takes advantage of both *bulk* gas flow and also *diffusion* of CO2 into the dead space while the lung is held open. This diffusion *reduces the dead space*, making ventilation more efficient and thereby reducing the necessary minute ventilation. Reducing the minute ventilation reduces the work the patient needs to expend and also reduces the energy that lung tissue must absorb during ventilation.
2. Incidentally, this suggests a different way to protocolize APRV which might be simpler and safer than most current protocols. Rather than hyper-sophisticated strategies for adjusting T-Low (e.g. based on peak expiratory flow rate angle), it would be simpler to adjust T-Low to target a tidal volume of 6-8 ml/kg. That is simple, easy, and supported by a fair amount of evidence (compared to many APRV protocols which are confusing, complicated, and not strongly evidence-based).

Image credits: Punching bag image from Wikipedia.

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Josh is the creator of PulmCrit.org. He is an associate professor of Pulmonary and Critical Care Medicine at the University of Vermont.